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Proposed Registration Decision PRD2012-26

Mono- and Di-Potassium Salts of Phosphorous Acid (Rampart)

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Overview

Proposed Registration Decision for Mono- and Di-Potassium Salts of Phosphorous Acid

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Rampart Technical and Rampart Fungicide, containing the technical grade active ingredient mono- and di-potassium salts of phosphorous acid, to control late blight and pink rot on post-harvest potatoes and to suppress downy mildew in brassica leafy vegetables and grapes.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Rampart Technical and Rampart Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on mono- and di-potassium salts of phosphorous acid, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on mono- and di-potassium salts of phosphorous acid, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Are Mono- and Di-Potassium Salts of Phosphorous Acid?

Mono- and di-potassium salts of phosphorous acid are fungicide active ingredients belonging to Group 33 as designated by the Fungicide Resistance Action Committee and are classified as phosphonates. The mode of action of phosphorous acid involves the induction of host plant resistance and the inhibition of energy metabolism in susceptible fungal pathogens. Mono- and di-potassium salts of phosphorous acid are the active ingredients contained in Rampart Fungicide.

Health Considerations

Can Approved Uses of Mono- and Di-Potassium Salts of Phosphorous Acid Affect Human Health?

Mono- and di-potassium salts of phosphorous acid are unlikely to affect human health when used according to label directions.

Exposure to mono- and di-potassium salts of phosphorous acid may occur when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example,

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Mono- and di-potassium salts of phosphorous acid are of low toxicity by the oral, dermal and inhalation routes, mildly irritating to the eyes, non-irritating to the skin, and are not a dermal sensitizer. The available information suggests that it is unlikely to have any short-term or prenatal developmental effects, as well as any significant genotoxic effects. The precautionary label statement indicating that contact with skin, eyes, and clothing must be avoided, and the personal protective equipment statement that applicators and other handlers must wear a long-sleeved shirt, long pants, gloves, shoes plus socks, and protective eyewear are effective mitigative measures to reduce the risk associated with the use of mono- and di-potassium salts of phosphorous acid.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Dietary risk to humans is considered negligible based on a long history of use and the low toxicity of the end use product. The available literature suggests that there is no toxicological concern from ingestion of the end-use product residues.

It is anticipated that the proposed uses of mono- and di-potassium salts of phosphorous acid in Canada on food crops will not pose a risk to any segment of the population, including infants, children, adults and seniors, from consumption of produce from treated crops. In the United States, phosphorous acid has been designated Generally Regarded As Safe (GRAS) and the potassium salts of phosphoric acid have been exempted from the requirement of tolerance in and on all food commodities when used as an agricultural fungicide on food crops. The United States Environmental Protection Agency (USEPA) introduced an initiative whereby an exemption from the requirement of tolerance was established for ammonium, sodium, and potassium salts of phosphorous acid on all food commodities to permit post-harvest application to stored potatoes at 35,600 ppm or less of phosphorous acid.

No risk due to exposure from drinking water is anticipated as the end-use product is not to be applied near or directly to water and is likely to be degraded in the environment.

Occupational Risks From Handling Rampart Fungicide

Occupational exposure to individuals mixing, loading, or applying Rampart Fungicide is not expected to result in unacceptable risk when the end-use product is used according to label directions.

Precautionary (for example, wearing of personal protective equipment) and hygiene statements on the label are considered adequate to protect individuals from occupational exposure. Since the application is done by commercial applicators, exposure to bystanders is expected to be negligible.

Environmental Considerations

What Happens When Mono- and Di-Potassium Salts of Phosphorous Acid Are Introduced Into the Environment?

Mono- and di-potassium salts of phosphorous acid are not expected to pose a risk to the environment when used as a fungicide.

Mono- and di-potassium salts of phosphorous acid will enter the environment when used as a fungicide on brassica leafy vegetables, grapes and potatoes in storage. Mono- and di-potassium salts of phosphorous acid produce phosphite ions when in contact with water. Over time, in soil, phosphite ions can be directly taken up by plant roots, slowly transform to phosphate (a plant nutrient), or bind with other substances in the soil. When phosphite ions get into lakes and rivers, it is expected that the phosphite will remain in the water phase. Phosphorous, in the form of phosphite, is not expected to be used by aquatic plants as a nutrient, but there is evidence that it could be used by certain kinds of bacteria. Mono- and di-potassium salts of phosphorous acid are not expected to accumulate in fish or other animals. It is also not expected that mono- and di-potassium salts of phosphorous acid will pose a risk to non-target terrestrial and aquatic species given its low toxicity to these organisms.

Value Considerations

What Is the Value of Rampart Fungicide?

Rampart Fungicide is a non-conventional fungicide that controls potato late blight and pink rot when applied as a post-harvest treatment on potatoes. Foliar applications of Rampart Fungicide also suppress downy mildew on grape and brassica leafy vegetables.

Rampart Fungicide is a fully systemic product with a low risk of pest resistance development. These characteristics make it a valuable option for integration into spray programs.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Rampart Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

The statement, "CAUTION - EYE IRRITANT" is required on the principal display panel of the end-use product label. Moreover, other precautionary statements on the end-use product label, such as: "Avoid breathing vapors or spray mist, avoid contact with eyes, skin or clothing; remove contaminated clothing and wash clothing before use; applicators and/or other handlers must wear protective eyewear, long pants and long sleeved shirt, waterproof gloves, and shoes plus socks," should be effective in minimizing the potential for exposure.

Next Steps

Before making a final registration decision on mono- and di-potassium salts of phosphorous acid, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on mono- and di-potassium salts of phosphorous acid (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

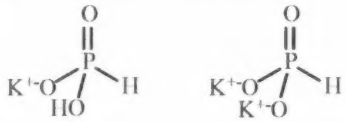
Science Evaluation

Mono and di-potassium salts of phosphorus acid

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance

Function	Fungicide	
Chemical name		
1. International Union of Pure and Applied Chemistry (IUPAC)	Monopotassium phosphonate and Dipotassium phosphonate	
2. Chemical Abstracts Service (CAS)	Phosphonic acid, monopotassium salt and Phosphonic acid, dipotassium salt	
CAS number	Monopotassium phosphonate Dipotassium phosphonate	13977-65-6 13492-26-7
Molecular formula	Monopotassium phosphonate KH_2PO_3 Dipotassium phosphonate	 K_2HPO_3
Molecular weight	Monopotassium phosphonate 120.09 Dipotassium phosphonate	 158.19
Structural formula		
	13977-65-6	13492-26-7
Purity of the active ingredient	53%	

1.2 Physical and Chemical Properties of the Active Ingredients and End-use Product

Technical Product—Rampart Technical

Property	Result
Colour and physical state	Colourless liquid
Odour	Odourless
Melting range	Not applicable
Boiling point or range	100°C
Density	1.41 g/mL
Vapour pressure at 20°C	The product is an aqueous liquid
Ultraviolet (UV)-visible spectrum	The product is not likely to absorb above 300 nm
Solubility in water at 20°C	Miscible
Solubility in organic solvents	Insoluble in most organic solvents
n-Octanol–water partition coefficient (K_{ow})	Not applicable. The product is insoluble in n-octanol
Dissociation constant (pK_a)	The mono- and di-potassium phosphites are essentially completely dissociated in aqueous solution
Stability (temperature, metal)	Unstable to metal and metal ions (iron powder, ferric chloride, lead shot and lead nitrate)

End-use Product—Rampart Fungicide

Property	Result
Colour	Colourless
Odour	Odourless
Physical state	Liquid
Formulation type	Solution
Guarantee	53 %
Container material and description	HDPE plastic jug, Bulk tote from 9.46L to 1000L
Density	1.41 g/mL
pH of 1% dispersion in water	6.3
Oxidizing or reducing action	The product is neither an oxidant nor a reductant
Storage stability	Unstable to metal and metal ions (iron powder, ferric chloride, lead shot and lead nitrate). The product is packaged in HDPE plastic containers and is expected to be stable.
Corrosion characteristics	The product is not expected to be corrosive
Explodability	The product is not expected to be explosive

1.3 Directions for Use

Rampart Fungicide is intended for post-harvest control of late blight and pink rot on potato, when applied once as a spray or rinse prior to storage or as an application through the humidification system in storage. Rampart Fungicide may also be applied as a foliar spray for suppression of downy mildew on grape (2.5-5 L/ha) and brassica leafy vegetables (3-7 L/ha) at 7-21 day intervals.

1.4 Mode of Action

Mono- and di-potassium salts of phosphorous acid have systemic activity. Their mode of action involves the induction of host plant resistance and the inhibition of energy metabolism in susceptible fungal pathogens.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Rampart Technical have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the submitted data for mono- and di-potassium salts of phosphorous acid was conducted. The submitted toxicity studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is adequate to qualitatively assess the toxicological hazards of this pest control product.

The submitted toxicology studies generated with a formulation (Fosphite, 53.0% w/w mono- and di-potassium salts of phosphorous acid) representing Rampart Technical and Rampart Fungicide, suggest that mono- and di- potassium salts of phosphorous acid are of low acute toxicity by oral, dermal, and inhalation routes of exposure, mildly irritating to the eyes, non-irritating to the skin, and are not a dermal sensitizer. The toxicology profile of Fosphite indicates that the technical product and the associated end-use product are of low toxicological concern.

Information on short-term toxicity, developmental toxicity (prenatal), and genotoxicity were not available for mono- and di-potassium salts of phosphorous acid at the time of evaluation. However, based on the general toxicological information on mono- and di-potassium salts of phosphorous acid together with a long history of safe use as a commodity chemical and its use as a pesticide in Australia and the United States, it appears unlikely that treatment related effects will result from exposure to mono- and di-potassium salts of phosphorous acid.

3.1.1 Incident Reports

Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the Health Canada website. Incidents from Canada were searched for pesticide products containing the active ingredient mono- and di-potassium salts of phosphorous acid.

As of June 27, 2012, there has been one human incident reported to the PMRA involving the active ingredient mono- and di-potassium salts of phosphorous acid. In this Human Minor incident, it is highly probable that the symptoms of irritated eye and altered taste in the mouth were related to exposure to the end-use product containing mono- and di-potassium salts of phosphorous acid which splashed into the eyes and mouth.

Although the information from the incident report supported the current toxicity database for mono- and di-potassium salts of phosphorous acid, it did not impact the risk assessment for this technical grade active ingredient. The toxicology profile of the technical grade active ingredient indicates that it is mildly irritating to eyes and it is of low acute toxicity by the oral route.

3.2 Food Residue Exposure Assessment

Rampart Fungicide is proposed for uses on potatoes, grapes and brassica leafy vegetables. A pre-harvest interval of one day is proposed for crops treated with Rampart Fungicide.

Due to the low toxicity of mono- and di-potassium salts of phosphorous acid, and its long history of use as an agrochemical, no adverse effects are anticipated from the presence of residues on food. In the United States, phosphorous acid is classified by the Food and Drug Administration as Generally Regarded as Safe (GRAS). The salts of phosphorous acid have been exempted from the requirement of tolerance in, and on, all food commodities when used as an agricultural fungicide on food crops.

There is reasonable certainty that no harmful effects will result from dietary exposure to residues of mono- and di-potassium salts of phosphorous acid from the proposed uses on food crops in the general population and potentially sensitive subpopulations, including infants and children.

Furthermore, while good hygiene practices, such as washing food produce prior to consumption, are not considered in the assessment for the registration of a food-use pesticide, they are recommended as any remaining residues are likely to be reduced by washing and possible cooking of treated crop before eating.

3.2.1 Drinking Water

Although the end-use product will be used for agricultural crops outdoors, as well as in contained treatment areas, it is not to be applied near or directly to water, and is likely to be degraded in the environment rapidly. No risk due to exposure from drinking water is anticipated.

3.2.2 Maximum Residue Limits

The promulgation of an maximum residue limit (MRL) for mono- and di-potassium salts of phosphorous acid and establishment of an acceptable daily intake was not required because of: 1) low oral toxicity of mono- and di-potassium salts of phosphorous acid, 2) Division B.15.002(2) of the Food and Drug Regulations provides a list of seven agricultural chemicals which are exempt from the requirement of setting an MRL, one of which is, mono- and dibasic sodium, potassium, and ammonium phosphate, 3) phosphorous acid has been designated Generally Regarded As Safe (GRAS) and the potassium salts of phosphoric acid have been exempted from the requirement of tolerance in and on all food commodities when used as an agricultural fungicide on food crops in the United States, and 4) there are no Codex MRLs established for mono- and di-potassium salts of phosphorous acid.

3.3 Occupational Exposure and Risk Assessment

3.3.1 Use Description

Rampart Fungicide is intended for use indoors for post-harvest application to potatoes before storage or to potatoes in storage and outdoors for foliar applications to grapes and brassica leafy vegetables. The proposed application methods include boom sprayers for foliar application and automated enclosed spray chamber system or humidifier for treating potatoes.

3.3.2 Mixer, Loader and Applicator Exposure and Risk Assessment

Occupational exposure to the mixer, loader, and applicator, as well as those responsible for clean-up and maintenance activities is anticipated to be minimal. Workers will be primarily exposed by dermal routes during handling, application, and re-entering freshly treated areas. Applicator exposure pertains only to foliar application, and there is potential for inhalation exposure to applicators from spray drift.

The end-use product label has a number of statements (for example, wearing of personal protective equipment, clothing, hygiene statement) to protect mixers, loaders and applicators against any unnecessary risk from exposure. The label instructs that applicators and other handlers must wear protective eyewear, long pants and long sleeved shirt, waterproof gloves, and shoes plus socks; also, avoid breathing of vapors or spray mist, avoid contact with eyes, skin or clothing; remove contaminated clothing and wash clothing before reuse, which should be effective in minimizing the potential for exposure.

Significant risk from exposure to mono- and di-potassium salts of phosphorous acid for the mixer, loader and applicator, as well as those responsible for clean-up, maintenance and repair activities is not anticipated due to the low toxicity of the active ingredient and reduced occupational exposure when label directions are followed.

3.3.3 Bystander Exposure

As the commercial application involves only authorized personnel, bystander exposure is expected to be negligible when the end-use product is used according to the label directions.

3.3.4 Postapplication Exposure

Postapplication exposure is possible when people enter the treated area soon after the application. The primary route of exposure for re-entry workers/individuals is dermal from contact with freshly treated surfaces. A restricted-entry interval of four hours proposed on the end-use product label will mitigate the potential for post-application exposure when occupational workers follow the label directions. Moreover, the end-use product has low dermal toxicity and low irritation potential, which limit unnecessary risk to individuals from postapplication exposure.

4.0 Impact on the Environment

Mono- and di-potassium salts of phosphorous acid have a low toxicity profile and a long history of use and, as such, a reduced database (including only acute toxicity information) was deemed sufficient to characterize the potential risks to the environment from the use of this fungicide.

4.1 Fate and Behaviour in the Environment

Mono- and di-potassium salts of phosphorous acid are highly soluble in water and will rapidly dissociate to yield hydrogen and phosphite ions. As a result, the phosphite ions will be readily removed from plant surfaces by rain wash-off. Over time, in soil, phosphite ions can be taken up directly by plant roots (as various salts), transformed to different oxidation states such as phosphate (an available form of phosphorous for plant nutrition), or can be bound up with other substances in soil. The conversion of phosphites to phosphates through microbial transformation in soil is, however, very slow. When phosphite enters aquatic systems, it is expected to remain in the water and not move to the sediment. Phosphite is not expected to be used as a nutrient (source of phosphorous) by aquatic plants and algae. There is, however, evidence indicating that

certain microorganisms are able to metabolise this form of phosphorous. Mono- and di-potassium salts of phosphorous acid are insoluble in octanol which, therefore, suggests that it would not bioaccumulate in fish or other animals.

4.2 Environmental Risk Characterization

A qualitative risk assessment was conducted using the submitted information on the toxicity of mono- and di-potassium salts of phosphorous acid to non-target organisms (aquatic and terrestrial).

Environmental toxicology data for mono- and di-potassium salts of phosphorous acid are summarized in Appendix I, Table 2.

4.2.1 Risks to Terrestrial Organisms

No effects were noted for honeybees (contact exposure) and birds (acute oral and dietary exposures) when exposed to a mono- and di-potassium phosphite solution up to concentrations much higher than those expected to be found in the environment following the use of mono- and di-potassium salts of phosphorous acid as a fungicide. No phytotoxic effects were noted in food crops when exposed to phosphite through soil drench. When exposed through foliar spray, slight leaf damage (<2% of leaf area affected, which is not expected to significantly affect the overall health of the plant) was observed in one of the food crops tested (bell pepper). Therefore, given the low toxicity observed in laboratory studies, mono- and di-potassium salts of phosphorous acid are not expected to pose a risk to non-target terrestrial organisms.

4.2.2 Risks to Aquatic Organisms

No effects were noted for *Daphnia magna* when exposed to high concentrations of a mono- and di-potassium phosphite solution. This compound was also not acutely toxic to the rainbow trout (*Oncorhynchus mykiss*). Therefore, given the low toxicity observed in laboratory studies, mono- and di-potassium salts of phosphorous acid are not expected to pose a risk to non-target aquatic organisms.

4.2.3 Incident reports

No incidents are reported in the PMRA database or the USEPA Ecological Incident Information System (EIIS) for mono- and di-potassium salts of phosphorous acid (USEPA OPP Chemical Code 076416).

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

5.1.1.1 Post-harvest control of potato late blight (*Phytophthora infestans*) and pink rot (*Phytophthora erythroseptica*)

A total of 15 field trials testing mono- and di-potassium salts of phosphorous acid or related active ingredients were submitted in support of the proposed claims. Mono- and di-potassium salts of phosphorous acid applied at rates close to the proposed rate consistently controlled late blight and pink rot incidence (≥90% reduction) on potato tubers under high disease pressure. Mono- and di-potassium salts of phosphorous acid was statistically comparable to the commercial standard in terms of efficacy. Based on these trial results, Rampart Fungicide is supported for control of potato late blight and pink rot, when applied once prior to or after storage. Rampart Fungicide is to be diluted in water (190 mL/L water). Two liters of this solution is to be applied to 1000 kg harvested potatoes.

5.1.1.2 Foliar applications for suppression of downy mildew (*Plasmopara viticola*) on grape

Five field trials were provided in support of the proposed claim. One trial was conducted in Ontario in 2008, and the four other studies were conducted in Australia in 1998. In the Ontario trial, nine mono- and di-potassium salts of phosphorous acid applications were made at 4.3 L/ha, resulting in control of disease severity under high disease pressure. In the remaining studies, mono- and di-potassium salts of phosphorous acid were sprayed three or four times at rates close to the lower label rate of 2.5 L/ha. Mono- and di-potassium salts of phosphorous acid treatments significantly reduced the number of sporulating leaves at the suppression level in comparison to the untreated controls. The use of Rampart Fungicide is supported for suppression of downy mildew on grape at 2.5-5.0 L/ha.

5.1.1.3 Foliar applications for suppression of downy mildew (*Hyaloperonospora parasitica*) on brassica leafy vegetables

Four field trials from the Southern U.S. States were carried out on broccoli, Chinese broccoli and collard in support of the proposed claim. Mono- and di-potassium salts of phosphorous acid or related active ingredients suppressed downy mildew when applied three to six times at rates equivalent to 2.3-7.6 L/ha on a 5-25 day schedule. Disease incidence and severity were reduced by an average of 42% and 62%, respectively. Based on the biological similarities among brassica leafy vegetables, the use of Rampart Fungicide is supported for suppression of downy mildew on the entire crop group.

5.2 Economics

No market analysis was performed for this product.

5.3 Sustainability

5.3.1 Survey of Alternatives

Refer to Appendix I, Table 3 for a summary of the active ingredients currently registered for the uses supported with Rampart Fungicide.

5.3.2 Compatibility with Current Management Practices Including Integrated Pest Management

Adequate cultural practices and sanitation measures are important means to prevent disease development in crops. Rampart Fungicide will not interfere with these preventative measures when used as directed.

5.3.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

According to the Fungicide Resistance Action Committee, phosphonate fungicides such as mono- and di-potassium salts of phosphorous acid (Group 33) present a low risk of pest resistance development. Consequently, the integration of Rampart Fungicide into spray programs may overall contribute to sound resistance management.

5.3.4 Contribution to Risk Reduction and Sustainability

Rampart Fungicide is effective in suppressing major oomycetes diseases, i.e. late blight and pink rot on stored potatoes as well as downy mildew on grape and brassica leafy vegetables. Rampart Fungicide contains mono- and di-potassium salts of phosphorous acid, a non-conventional active ingredient that exhibits systemic properties as well as a low risk of pest resistance development. These characteristics make it a valuable option for the management of high-risk pathogens such as *Plasmopara viticola* and *Hyaloperonospora parasitica* in crops where a limited number of alternatives are registered. Furthermore, Rampart Fungicide can be applied up to the day before harvest. Conversely to certain conventional fungicides used on grape, Rampart Fungicide is not subject to long re-entry and pre-harvest intervals.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e. persistent (in air, soil, water and/or sediment), bio accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, mono- and di-potassium salts of phosphorous acid was assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

Mono- and di-potassium salts of phosphorous acid do not meet Track 1 criteria, and are not considered Track 1 substances. These are inorganic substances. Mono- and di-potassium salts of phosphorous acid are insoluble in octanol and are, therefore, not expected to bioaccumulate in the environment.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02,[8] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

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5 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*.

6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

8 DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

- Technical grade Rampart Technical and the end-use products Rampart Fungicide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

7.0 Summary

7.1 Human Health and Safety

The available information for mono- and di-potassium salts of phosphorous acid is adequate to qualitatively identify the toxicological hazards that may result from human exposure to mono- and di-potassium salts of phosphorous acid. Submitted information suggests that mono- and di-potassium salts of phosphorous acid are of low acute toxicity irrespective of the route of exposure, mildly irritating to the eyes, non-irritating to the skin, and are not a skin sensitizer.

Although occupational exposure is expected, the precautionary statements on the end-use product label are sufficient to minimize any risk due to exposure of workers and bystanders.

Exposure to mono- and di-potassium salts of phosphorous acid from the diet or drinking water is not expected to be of concern. The PMRA did not require a maximum residue limit (MRL) to be established for mono- and di-potassium salts of phosphorous acid.

7.2 Environmental Risk

The use of mono- and di-potassium salts of phosphorous acid as a fungicide, according to the Rampart Fungicide label is not expected to pose a risk to terrestrial or aquatic non-target organisms.

7.3 Value

The submitted value information is adequate to support the following claims:

- post-harvest treatment for control of late blight and pink rot on stored potatoes
- foliar applications for suppression of downy mildew on grape
- foliar applications for suppression of downy mildew on brassica leafy vegetables

7.4 Unsupported Uses

All uses were supported (see Appendix 1, Table 4).

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Rampart Technical and Rampart Fungicide, containing the technical grade active ingredient mono- and di-potassium salts of phosphorous acid, to control late blight and pink rot on post-harvest potatoes and to suppress downy mildew in brassica leafy vegetables and grapes.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

°C	degree(s) Celsius
µg	micrograms
µm	micrometre(s)
a.i.	active ingredient
bw	body weight
CAS	Chemical Abstracts Service
C.I.	confidence interval
cm^2	centimetre(s) squared
d	day(s)
EC_{25}	effective concentration on 25% of the population
g	gram
GRAS	Generally Regarded as Safe
h	hour(s)
ha	hectare(s)
HDPE	High density polyethylene
hr(s)	hour(s)
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	*n*-octanol–water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
mg	milligram
mL	millilitre
MAS	maximum average score
MIS	maximum irritation score
MRL	maximum residue limit
NOEC	no observed effect concentration
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet
w/w	weight per weight dilution

Appendix I Tables and Figures

Table 1 Toxicity Profile of Fosphite (mono- and di-potassium salts of phosphorous acid 53% w/w)

Study	Species/Strain Doses	Result	Target Organ/Significant Effects/Comments	Reference
Oral	Wistar albino rats 5 rats/sex/dose by gavage 5000, 4000, 3500, 2000 mg/kg bw	LD_{50} ♂ & ♀: > 2000 mg/kg bw	No mortality at the lowest dose tested. Piloerection, lacrimation, ataxia, lethargy, and ano-genital staining were noticed at tested doses. No gross abnormalities were noted at necropsy in the lowest dose tested. **Low acute oral toxicity**	2082062
Dermal	New Zealand white rabbits 5 rabbits/sex/dose 2000 mg/kg bw applied for 24 hrs	LD_{50} ♂ & ♀: > 2000 mg/kg bw	No mortality or treatment-related effects. No gross abnormalities were noted at necropsy. **Low acute dermal toxicity**	2082063
Inhalation (whole-body exposure)	Wistar albino rats 5 rats/sex/dose Gravimetric chamber concentration of 2.2 mg/L, mass median aerodynamic diameter of 1.4 µm, and exposure period of 4 hrs	LC_{50} ♂ & ♀ > 2.2 mg/L	No mortality. Instances of chromorhinorrhea, chromodacryorrhea were noted through day 4. All animals appeared normal from day 5 through Day 14. Necropsy findings were normal. **Low acute inhalation toxicity**	2082064
Primary eye irritation (Draize method)	New Zealand white rabbits 6 rabbits (♂)/dose Dosed with 0.1mL of the test substance and left unwashed. Ocular irritation was scored at 1, 24, 48 and 72 hours post-instillation.	MAS [a] = 2/110 MIS [b] = 17/110 (1hr)	No corneal opacity. Iritis and conjunctival irritation observed in all treated eyes were resolved by 24 hours and 72 hours of the treatment, respectively. **Mildly irritating to the eye** (Based on an MIS of 17/110 at 1 hr)	2082065
Primary dermal irritation (Draize method)	New Zealand white rabbits 6 rabbits (♂)/dose 0.5 ml of the test substance applied to one 6-cm^2 intact dose site per animal for 4 hr exposure under occlusion	MAS [a] = 0/8 MIS [b] = 0/8	There was no erythema or edema noticed at any observation period. **Non-irritating to the skin**	2082066

Study	Species/Strain Doses	Result	Target Organ/Significant Effects/Comments	Reference
Dermal Sensitization (Buehler Method) Scored at 24 and 48 hrs after each induction Scored at 24, 48 and 72 hrs after challenge application	Hartley-Albino Guinea pigs 15 (♂) Naïve control: 5 animals Treatment group (Dosed with 0.4 ml of the test substance, once/week for a 3-week period): 10 animals Animals were challenged 14 days after the last induction exposure with a dose of 0.4 ml test substance.	Negative results	No treatment related effects were observed. Erythema was absent at induction and challenge phases. Historical positive control validation study validates the test system of this study. **Negative skin sensitizer**	2082067

[a] MAS = Maximum Average Score for 24, 48 and 72 hrs
[b] MIS = Maximum Irritation Score (average)

Table 2 Toxicity to Non-Target Species

Organism	Exposure	Test substance[a]	Endpoint value	Degree of toxicity[b]	Reference
Terrestrial					
Invertebrates					
Bee (*apis mellifera*)	48h-Contact	Fosphite	LD_{50} >25 µg a.i./bee	Relatively non-toxic	2011310
Birds					
Bobwhite quail (*Colinus virginianus*)	Acute	Fosphite	LD_{50} > 2000 mg a.i./kg bw	Practicall y non-toxic	2011314
Mallard (*Anas platyrhynchos*)	8d-Dietary	Fosphite	LC_{50} >5000ppm (LD_{50} > 1594.4 mg a.i./kg bw/day)	Practicall y non-toxic	2011315
Plants[c]					
Celery, cotton, onion, strawberry, tomato	Soil drench	Fosphite	EC_{25} >10.5 kg a.i./ha	N/A	2011316
potato, strawberry, eggplant, tomato, lettuce, cucumber, grapes, apple, avocado, Bell pepper	Foliar spray	Fosphite	EC_{25} >5.2 kg a.i./ha	N/A	2011317

Organism	Exposure	Test substance[a]	Endpoint value	Degree of toxicity[b]	Reference
Aquatic					
Freshwater species					
Daphnia magna	48h-Acute	Fosphite	LC_{50} > 1200 mg a.i./L	Practically non-toxic	2011312
Rainbow trout (*Oncorhynchus mykiss*)	96h-Acute	Fosphite	LC_{50} = 790 mg a.i./L (95%C.I.:630-110 mg a.i./L) NOEC = 370 mg a.i./L	Practically non-toxic	2011313

[a] The active tested, mono- and di-potassium phosphite is reported as Fosphite in the studies; guarantee is 53% mono- and di-potassium phosphite

[b] Atkins *et al.*(1981) for bees and US EPA classification for others, where applicable

[c] Non-guideline studies

Table 3 Summary of Fungicide Alternatives for the Uses Supported with Rampart Fungicide

Crop / Crop group	Disease	Active Ingredient and Resistance Management Group
Potato (post-harvest)	Late blight, pink rot	***Conventional***: N/A
		Non-conventional: mono- and di-basic sodium, potassium and ammonium phosphites (33)

Crop / Crop group	Disease	Active Ingredient and Resistance Management Group
Grape	Downy mildew	***Conventional***: metalaxyl (4) + mancozeb (M3) boscalid (7) + pyraclostrobin (11) kresoxim-methyl (11) zoxamide (22) zoxamide (22) + mancozeb (M3) dinocap (29) + mancozeb (M3) dimethomorph (40) dimethomorph (40) + ametoctradin (45) mandipropamid (40) fluopicolide (43) ametoctradin (45) copper (M3) mancozeb (M3) metiram (M3) captan (M4) folpet (M4)
		Non-conventional: citric acid + lactic acid (NC) mono- and di-basic sodium, potassium and ammonium phosphites (33)
Brassica leafy vegetables*	Downy mildew	***Conventional***: boscalid (7) + pyraclostrobin (11) fenamidone (11) fosetyl-al (33) dimethomorph (40) mandipropamid (40) dimethomorph (40) + ametoctradin (45) fluopicolide (43) copper (M3) chlorothalonil (M5)
		Non-conventional: mono- and di-basic sodium, potassium and ammonium phosphites (33) *Bacillus subtilis* strain QST 713 (44)

* Certain alternatives listed in this table are registered exclusively on specific commodities from this crop group.

Table 4 Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Proposed claim	VSAD comments
Potato: control of late blight (*Phytophthora infestans*) and pink rot (*Phytophthora erythroseptica*) with one post-harvest application. Dilute 190 mL Rampart Fungicide in 1 L water. Application prior to storage of potato tubers: Apply 2 L of this solution as a spray or rinse per 1000 kg of harvested potato prior to storage. Application to stored potatoes: Inject 2 L of this solution per 1000 kg of stored potato tubers into water used for post-harvest storage.	Supported.
Grape: suppression of downy mildew (*Plasmopara viticola*) with five foliar applications at 2.5-5.0 L/ha on a 7-21 day schedule.	Supported.
Brassica leafy vegetables (broccoli, Brussels sprout, cabbage, cauliflower, cavalo broccoli, collard, Chinese cabbage, Chinese mustard cabbage, kale, kohlrabi, mizuna, mustard greens, mustard spinach and rapegreens): suppression of downy mildew (*Peronospora parasitica*) with foliar applications at 3-7 L/ha on a 7-21 day schedule. For brassicas with one crop cycle per season, do not make more than eight applications of Rampart Fungicide per season on a given area. For brassicas with multiple crop cycles per season, do not make more than three applications of Rampart Fungicide per crop cycle, with a maximum of 12 applications per season on a given area.	Supported.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
2011288	Fosphite- Fungicide Formulation, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.12.1,2.13.1,2.13.2
2011291	Detailed Production Process Description, DACO: 2.11.3
2011289	Certificate of Analysis – [CBI removed], DACO: 2.11.3
2011290	Product Specification [CBI removed], DACO: 2.11.3
2011293	Batch data, DACO: 2.13.3
2011295	Batch data, DACO: 2.13.3
2011296	Batch data, DACO: 2.13.3
2011297	Batch Analysis of Phosgard, DACO: 2.13.3
2011285	Comprehensive Data Summary for Rampart Technical and Rampart Fungicide, DACO: 12.7
2011298	Chemical and Physical Properties, DACO: 2.14, 2.14.1, 2.14.10, 2.14.11, 2.14.12, 2.14.13, 2.14.14, 2.14.2, 2.14.3, 2.14.4, 2.14.5, 2.14.6, 2.14.7, 2.14.8, 2.14.9
2011299	Summary of the Results of Chemical Stability Studies of Phosgard, DACO: 2.14.14

2.0 Human and Animal Health

PMRA Document Number	Reference
2082062	1998, Single Dose Oral Toxicity in Rats/LD 50 in Rats, DACO: 4.2.1,4.6.1
2082063	1998, Acute Dermal Toxicity in Rabbits/LD 50 in Rabbits, DACO: 4.2.2,4.6.2
2082064	1998, Acute Inhalation Toxicity in Rats/LC 50 in Rats, DACO: 4.2.3,4.6.3

2082065 1998, Primary Eye Irritation/Corrosion in Rabbits, DACO: 4.2.4,4.6.4

2082066 1998, Primary Dermal Irritation in Rabbits, DACO: 4.2.5,4.6.5

2082067 1998, Delayed Contact Dermal Sensitization Test - Buehler Method, DACO: 4.2.6,4.6.6

2011347 2009, Material Data Safety Sheets Rampart Fungicide, DACO: 0.9

2011364 2011, Metabolism Waiver for Rampart Fungicide, DACO: 6.1

2011363 2011, 5.2 Use Description for Rampart Fungicide, DACO: 5.2

3.0 Environment

PMRA Document Number **Reference**

2011309 2010, Summary of Environmental Toxicology, DACO: 9.1, 9.2.1, 9.3.1, 9.5.1, 9.6.1, 9.8.1, 9.8.5

2011310 1999, Fosphite – Acute Contact Toxicity Test with Honey Bees (*Apis mellifera*), DACO: 9.2.4.2

2011312 1999, Fosphite - Acute Toxicity to Daphnids (*Daphnia magna*) under static conditions, DACO: 9.3.2

2011313 1999, Fosphite - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) under static conditions, DACO: 9.5.2.1

2011314 1999, Avian Acute Oral Toxicity Test in Bobwhite quail with Fosphite (53% Mono- and Di-Potassium Phosphite Solution), DACO: 9.6.2.1

2011315 1999, Acute Avian Dietary Toxicity (LC_{50}) study in Mallard Ducklings with Fosphite (Mono- and Di-Potassium phosphite), DACO: 9.6.2.5

2011316 2010, Phytotoxicity Observations: Different Fosphite Rates on Food Crops, Soil Application, DACO: 9.8.4

2011317 2010, Phytotoxicity Observations: Different Fosphite Rates on Food Crops, DACO: 9.8.4

4.0 Value

PMRA Document Number	Reference
2011351	2011, Value Summary for Rampart Fungicide (Active ingredient Mono- and dipotassium salts of phosphorous acid) for suppression of downy mildew on leafy brassica crops (Crop subgroup 5B), and grapes and control of late blight and pink rot on stored potatoes, DACO: 10.1, 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.3, 10.3.1, 10.3.2, 10.5.1, 10.5.2, 10.5.3
2011352	2011, Excel Tables for Rampart on Grapes, Potatoes and Leafy Brassica Crops, DACO: 10.2.3.1

B. Additional Information Considered

i) Published Information

1.0 Environment

PMRA Document Number	Reference
2144530	T-4-121 – Requirements for Phosphite and Phosphorous Acid Materials Represented for Use as Fertilizers. Canadian Food Inspection Agency. http://www.inspection.gc.ca/plants/fertilizers/trade-memoranda/t-4-121/eng/1307910613324/1307910722202
2144638	Thao, H. T. B., Yamakawa, T. 2009. Phosphite (phosphorous acid): Fungicide, fertilizer or biostimulator? Soil Science and Plant Nutrition. 55: 228-234. DACO: 10.6